

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Attorney Docket No. 053466/0294**

In re patent application of

Toshihiko OHOMO et al.

Serial No. Divisional of 08/646,265

Filed: Concurrently Herewith

For: RESHAPED HUMAN TO HUMAN MEDULLOBLASTOMA CELLS

**PRELIMINARY AMENDMENT**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above application as follows:

**IN THE SPECIFICATION:**

Please amend the specification by inserting before the first line of text the following sentence:

--This application is a Divisional of application Serial No. 08/646,265, filed September 9, 1996, which is a national stage of PCT/JP94/01763, filed October 19, 1994.--

Page 14, Table 1, line 5, before "ONS-M21VL" insert -- (residues 21-76 of SEQ ID NO:27) --;

line 6, before "REI" insert -- (residues 1-38 of SEQ ID NO:112)--;

line 7, before "RVLba" insert -- (residues 1-55 of SEQ ID NO:43)--;

line 8, before "RVLb" insert -- (residues 1-55 of SEQ ID NO:47)--;

line 9, before "RVLc" insert -- (residues 1-55 of SEQ ID NO:51)--;

line 10, before "RVLd" insert -- (residues 1-55 of SEQ ID NO:53)--;

line 11, before "RVLe" insert -- (residues 1-55 of SEQ ID NO:57)--;  
line 12, before "RVLf" insert -- (residues 1-55 of SEQ ID NO:59)--;  
line 13, before "RVLg" insert -- (residues 1-55 of SEQ ID NO:63)--;  
line 14, before "RVLh" insert -- (residues 1-55 of SEQ ID NO:65)--;  
line 15, before "RVLi" insert -- (residues 1-55 of SEQ ID NO:69)--;  
line 16, before "RVLj" insert -- (residues 1-55 of SEQ ID NO:73)--;  
line 17, before "RVLk" insert -- (residues 1-55 of SEQ ID NO:75)--;  
line 18, before "RVLi" insert -- (residues 1-55 of SEQ ID NO:77)--;  
line 19, before "RVLm" insert -- (residues 1-55 of SEQ ID NO:81)--;  
line 20, before "RVLn" insert -- (residues 1-55 of SEQ ID NO:85)--;  
line 21, before "RVLo" insert -- (residues 1-55 of SEQ ID NO:87)--;  
line 22, before "RVLp" insert -- (residues 1-55 of SEQ ID NO:91)--.

Page 15, Table 2, line 5, before "ONS-M21VL" insert -- (residues 77-127 of SEQ ID NO:27)--;

line 6, before "REI" insert -- (residues 39-80 of SEQ ID NO:112)--;  
line 7, before "RVLa" insert -- (residues 56-106 of SEQ ID NO:43)--;  
line 8, before "RVLb" insert -- (residues 56-106 of SEQ ID NO:47)--;  
line 9, before "RVLc" insert -- (residues 56-106 of SEQ ID NO:51)--;  
line 10, before "RVLd" insert -- (residues 56-106 of SEQ ID NO:53)--;  
line 11, before "RVLe" insert -- (residues 56-106 of SEQ ID NO:57)--;  
line 12, before "RVLf" insert -- (residues 56-106 of SEQ ID NO:59)--;  
line 13, before "RVLg" insert -- (residues 56-106 of SEQ ID NO:63)--;

line 14, before “RVLh” insert -- (residues 56-106 of SEQ ID NO:65)--;  
line 15, before “RVLi” insert -- (residues 56-106 of SEQ ID NO:69)--;  
line 16, before “RVLj” insert -- (residues 56-106 of SEQ ID NO:73)--;  
line 17, before “RVLk” insert -- (residues 56-106 of SEQ ID NO:75)--;  
line 18, before “RVLi” insert -- (residues 56-106 of SEQ ID NO:77)--;  
line 19, before “RVLm” insert -- (residues 56-106 of SEQ ID NO:81)--;  
line 20, before “RVLn” insert -- (residues 56-106 of SEQ ID NO:85)--;  
line 21, before “RVLo” insert -- (residues 56-106 of SEQ ID NO:87)--;  
line 22, before “RVLp” insert -- (residues 56-106 of SEQ ID NO:91)--.

Page 17, Table 3, line 5 before “ONS-M21VH” insert -- (residues 20-2136 of SEQ ID NO:29)--;

line 6, before “EU” insert -- (SEQ ID NO:113)--;  
line 7, before “RVHa” insert -- (residues 23-139 of SEQ ID NO:109)--;  
line 21, before “ND” insert -- (SEQ ID NO:114)--.

Page 20, line 35, after “CDR1” insert -- (SEQ ID NO:115)--;  
line 36, after “CDR2” insert -- (SEQ ID NO:116)--.

Page 21, line 1, after “CDR1” insert -- (SEQ ID NO:117)--;  
line 5, after “CDR1” insert -- (SEQ ID NO:118)--;

line 6, after “CDR2” insert -- (SEQ ID NO:119)--;

line 7, after “CDR3” insert -- (SEQ ID NO:120)--;

line 12, delete “80” and insert --99--;

line 15, delete “40, 43, 46, 47, 50, 51, 54, 55, 58, 61, 62,” and insert --43,  
47, 51, 53, 57, 59, 63, 65, 69, 73, 75, 77, 81, 85, 87 or 91.--;

line 16, delete “63, 66, 69, 70 or 73.”

line 20, delete “80” and insert --99--;

line 23, delete “73” and insert --91--;

line 29, delete “90” and insert --111--‘

line 31, delete “89” and insert --109--.

Page, line 18, delete “27 and insert --28--.

Page 27, Table 4, line 3, delete “27” and insert --29--;

line 12, delete “28” and insert --30--;

line 14, delete “29” and insert --31--;

line 19, delete “30” and insert --32--;

line 20, delete “31” and insert --33--.

Page 29, line 18, delete “32” and insert --34--; delete “33” and insert --35--;

line 21, delete “34” and insert --36--;

line 22, delete “35” and insert --37--; delete “36” and insert --38--;

line 23, delete “37” and insert --39--; delete “38” and insert --40--;

line 24, delete “39” and insert --41--.

Page 30, line 32, delete “40” and insert --43--;

line 35, delete “41” and insert --44--;

line 36, delete “42” and insert --45--.

Page 31, line 14, delete “44” and insert --48--;

line 15, delete “45” and insert --49--;

line 20, delete “46” and insert --50 and 51--;

line 28, delete “47” and insert --52 and 53--;

line 30, delete "48" and insert --54--;

line 31, delete "49" and insert --55--;

line 37, delete "50" and insert --56 and 57--.

Page 32, line 10, delete "51" and insert --58 and 59--;

line 12, delete "52" and insert --60--;

line 13, delete "53" and insert --61--;

line 18, delete "54" and insert --62 and 63--;

line 24, delete "55" and insert --64 and 65--;

line 26, delete "56" and insert --66--;

line 27, delete "57" and insert --67--;

line 34, delete "58" and insert --68 and 69--;

line 36, delete "59" and insert --70--;

line 37, delete "60" and insert --71--.

Page 33, line 6, delete "61" and insert --72 and 73--;

line 12, delete "62" and insert --74 and 75--;

line 22, delete "63" and insert --76 and 77--;

line 24, delete "64" and insert --78--;

line 25, delete "65" and insert --79--;

line 33, delete "66" and insert --80 and 81--;

line 35, delete "67" and insert --82--;

line 36, delete "68" and insert --83--.

Page 34, line 5, delete "69" and insert --84 and 85--;

line 15, delete "70" and insert --86 and 87--;

line 17, delete “71” and insert --88--;

line 18, delete “72” and insert --89--;

line 23, delete “73” and insert --90 and 91--.

Page 35, line 10, delete “74 and 77” and insert --92 to 95--;

line 2, delete “74” and insert --92--;

line 13, delete “75” and insert --93--;

line 14, delete “76” and insert --94--; delete “77” and insert --95--;

line 23, delete “78” and insert --96--;

line 24, delete “79” and insert --97--.

Page 36, line 2, delete “80” and insert --98 and 99--.

Page 37, line 8, delete “90” and insert --111--.

Page 38, line 19, delete “83” and insert --102--;

line 23, delete “84” and insert --103--;

line 26, delete “85” and insert --104--;

line 30, delete “86” and insert --105--;

line 34, delete “87” and insert --106--.

Page 39, line 1, delete “88” and insert --107--.

Page 40, line 20, delete “89” and insert --108 and 109--.

Page 43, at the end of the specification, before the claims, insert the printed Sequence Listing submitted concurrently herewith, delete the Sequence Listing appearing on pages 44-87 of the as-filed specification, and renumber pages 1-52 of the Sequence Listing submitted concurrently herewith as pages 44-95 of the specification.

**IN THE CLAIMS:**

Please cancel claims 2-39 without prejudice or disclaimer.

Please add the following claims:

--40. A method for making a reshaped human antibody comprising complementarity determining regions derived from a mouse antibody and framework regions derived from a human antibody, wherein an amino acid residue 46 of L chain numbered according to Kabat et al. is a mouse antibody residue and the reshaped human antibody creates a functional antigen binding site.

41. The method of claim 40, wherein an amino acid residue 94 of H chain numbered according to Kabat et al. is an additional mouse antibody residue.

42. The method of claim 41, wherein amino acid residues 27, 28, 29 and 30 of H chain numbered according to Kabat et al. are additional mouse antibody residues.

43. The method of claim 40, wherein the amino acid residue 46 is proline.

44. A reshaped human antibody produced by the method of claim 40.

45. A reshaped human antibody produced by the method of claim 41.

46. A reshaped human antibody produced by the method of claim 42.

47. A reshaped human antibody produced by the method of claim 43.

48. A method for making a single-chain Fv region comprising a reshaped human antibody H chain V region and L chain V region, which are linked by a linker peptide, and have complementarity determining regions derived from a mouse antibody and framework regions derived from a human antibody, wherein an amino acid residue 46 of L chain V region numbered according to Kabat et al. is a mouse residue and the single chain Fv region creates a functional antigen binding site.

49. The method of claim 48, wherein an amino acid residue 94 of H chain numbered according to Kabat et al. is an additional mouse antibody residue.

50. The method of claim 49, wherein amino acid residues 27, 28, 29 and 30 of H chain numbered according to Kabat et al. are additional mouse antibody residues.

51. The method of claim 48, wherein the amino acid residue 46 is proline.

52. The method of claim 48, wherein the linker peptide has the following amino acid sequence:

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

53. A single-chain Fv region produced by the method of claim 48.

54. A single-chain Fv region produced by the method of claim 49.

55. A single-chain Fv region produced by the method of claim 50.

56. A single-chain Fv region produced by the method of claim 51.

57. A single-chain Fv region produced by the method of claim 52.--

### REMARKS

Applicants respectfully request entry of the foregoing amendment prior to the examination on the merits of the instant application. Should the Examiner have any questions or comments regarding the pending application or this preliminary amendment, the Examiner is requested to call the undersigned.

If there are any fees due in connection with the filing of this Preliminary Amendment, please charge the fees to our Deposit Account No. 19-0741.

Respectfully submitted,

Date: December 29, 2000

*Michael D. Kammerer,*  
Reg. No. 32,904, for  
Harold C. Wegner  
Reg. No. 25,258

**FOLEY & LARDNER**  
3000 K Street, N.W., Suite 500  
Washington, D.C. 20007-5109  
Telephone: (202) 672-5300  
Facsimile: (202) 672-5399

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